

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
10 September 2004 (10.09.2004)

PCT

(10) International Publication Number
WO 2004/075841 A3

(51) International Patent Classification⁷: **C07C 319/20**,
148/00, 149/273, 323/60

(21) International Application Number:
PCT/US2004/005265

(22) International Filing Date: 23 February 2004 (23.02.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/449,629 24 February 2003 (24.02.2003) US

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(81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
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TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Published:

- *with international search report*
- *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments*

(88) Date of publication of the international search report:
7 April 2005

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: PROCESS FOR PREPARING BENZHYDRYLTHIOACETAMIDE

(57) Abstract: The present invention is directed to an improved process for preparing modafinil wherein benzhydrylthioacetamide is prepared in high yield and purity by the reaction of a haloacetamide with the reaction product of thiourea and benzhydrol in aqueous solution. The reaction employing the haloacetamide is conducted in a solvent comprising water and an organic solvent such as dimethylformamide having dissolved therein a basic salt such as potassium carbonate. The resulting benzhydrylthioacetamide can be oxidized to provide the pharmaceutical modafinil.

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INTERNATIONAL SEARCH REPORT

International Application No

PC 7/US2004/005265

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C319/20 C07C148/00 C07C149/273 C07C323/60

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 2004/002547 A1 (LARGEAU DENIS ET AL) 1 January 2004 (2004-01-01) the whole document	1-13
X	EP 1 260 501 A (CHEMAGIS LTD) 27 November 2002 (2002-11-27) the whole document	1-13
A	WO 02/10125 A (GERSHON NEOMI ; SINGER CLAUDE (IL); TEVA PHARMA (IL); ARONHIME JUDITH) 7 February 2002 (2002-02-07) the whole document	1-13
A	US 4 177 290 A (LAFON LOUIS) 4 December 1979 (1979-12-04) the whole document	1-13

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

29 July 2004

Date of mailing of the international search report

11 02 2005

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/005265

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/005265

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-13

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-13

Process for preparing benzhydrylthioacetamide comprising reacting benzhydrylthiocarboxamidine salt with haloacetamide in a reaction medium comprising water, a water miscible organic solvent and a water soluble basic salt.

2. claims: 14-25

Process for preparing modafinil comprising: a) reacting benzhydrol with thiourea in the presence of hydrogen bromide to provide benzhydrylthiocarboxamidine bromide, b) reacting haloacetamide with the product of step a) to provide benzhydrylthioacetamide and c) oxidizing the product of step b) to obtain benzhydrylsulphonylacetamide wherein the reaction of step b) is conducted in a solvent comprising a water miscible organic solvent and water in the presence of a basic salt.

3. claims: 26-34

Process for the purification of modafinil which comprises contacting the crude modafinil with a halo-organic solvent and then separating the modafinil from the solvent.
